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12. (Amended) A pharmaceutical composition of claim 11, wherein the angiotensin converting enzyme inhibitor is alacepril, alatriopril, altiopril calcium, ancovenin, benazepril, benazepril hydrochloride, benazeprilat, benzoylcaptopril, captopril, captopril-cysteine, captopril-glutathione, ceranapril, ceranopril, ceronapril, cilazapril, cilazaprilat, delapril, delapril-diacid, enalapril, enalaprilat, enapril, epicaptopril, foroxymithine, fosfenopril, fosenopril, fosenopril sodium, fosinopril, fosinopril sodium, fosinoprilat, fosinoprilic acid, glycopril, hemorphin-4, idrapril, imidapril, indolapril, indolaprilat, libenzapril, lisinopril, lyciumin A, lyciumin B, mixanpril, moexipril, moexiprilat, moveltipril, muracein A, muracein B, muracein C, pentopril, perindopril, perindoprilat, pivalopril, pivopril, quinapril, quinapril hydrochloride, quinaprilat, ramipril, ramiprilat, spirapril, spirapril hydrochloride, spiraprilat, spiropril, spiropril hydrochloride, temocapril, temocapril hydrochloride, teprotide, trandolapril, trandolaprilat, utibapril, zabicipril, zabiciprilat, zofenopril or zofenoprilat.

13. (Amended) A pharmaceutical composition of claim 12, wherein the angiotensin converting enzyme inhibitor is ramipril, ramiprilat, lisinopril, enalapril or enalaprilat.

14. (Amended) A pharmaceutical composition of claim 11, wherein the angiotensin II antagonist is candesartan, candesartan cilexetil, losartan, valsartan, irbesartan, tasosartan, telmisartan, or eprosartan.

15. (Amended) A pharmaceutical composition of claim 14, wherein the angiotensin II antagonist is candesartan, or candesartan cilexetil.

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18. (New) A method as claimed in claim 4, wherein the patient exhibits normal or low blood pressure.

Remarks

I. Status of the claims

Claims 4-18 are pending in this application. The claims recite a method of preventing congestive heart failure in a patient having certain characteristics, and a composition for such treatment. Claims 4 and 10, the only independent claims now

in the application, recite that the patient has not previously had congestive heart failure and has an essentially maintained heart function. Support for this amendment appears in the specification at page 3 in the third full paragraph. Support for new claim 18, which recites that the patient exhibits normal or low blood pressure, finds support in the same paragraph.

II. Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1 and 3-15 under 35 U.S.C. § 112, first paragraph, as not enabling for "pharmaceutically acceptable derivatives" of ACE inhibitors. Although applicants do not acquiesce in the merits of the rejection, the claims have been amended to delete the phrase "pharmaceutically acceptable derivative."

The method and composition of claims 4 and 10 recite the presence of an inhibitor of the renin-angiotensin system. The phrase "pharmaceutically acceptable derivative" is unnecessary in those claims, because a compound is either an inhibitor of the renin-angiotensin system or it is not, and those skilled in the art are able to make that determination. To the extent that certain derivatives of specifically-named or known compounds are inhibitors of the renin-angiotensin system, those compounds are embraced by claims 4 and 10. The same reasoning applies to, for example, the scope of angiotensin converting enzyme inhibitors and angiotensin II type 1 receptor antagonists recited in claims 5 and 11. OK

III. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claim 2 under 35 U.S.C. § 112, second paragraph, as indefinite in the terminology "normal or low" blood pressure. In particular, the Examiner argued that one skilled in the art cannot determine what constitutes a normal or low blood pressure. Claim 2 has been canceled, so this rejection is moot. New claim 18, however, recites that the patient has normal or low blood pressure, and applicants address the rejection as it may pertain to this new claim. OK

Those skilled in the art do know what constitutes normal or low blood pressure. As noted in the specification in the last full paragraph on page 3, examples of guidelines defining blood pressure values for different patient groups

are issued by the WHO and JNC (USA). For the present invention a suitable definition of a normal or low blood pressure can be found in JNC VI, which is identified in the specification as well. Especially in light of these guidelines pointed out in the specification, the determination whether a patient has normal or low blood pressure is routine in the art. Applicants therefore respectfully request that the Examiner withdraw this rejection.

IV. Rejections under 35 U.S.C. § 102

The Examiner rejected certain claims directed to the prevention of stroke as anticipated by EP 0 474 438 to Sudilovsky. Applicants do not acquiesce in the conclusion of unpatentability reached by the Examiner. Nonetheless, applicants have canceled claims directed to the prevention of stroke, rendering this rejection moot. Applicants retain the right to pursue the canceled subject matter in a separate patent application.

The Examiner rejected certain claims directed to the prevention of diabetes as anticipated by EP 0 426 066 to Tschollar. Applicants do not acquiesce in the conclusion of unpatentability reached by the Examiner. Nonetheless, applicants have canceled claims directed to the prevention of diabetes, rendering this rejection moot. Applicants retain the right to pursue the canceled subject matter in a separate patent application.

The Examiner rejected claim 4 directed to the prevention of congestive heart failure as anticipated by WO 96/24373 to Maclaughlan et al. ("Maclaughlan"). In support of the rejection, the Examiner stated that Maclaughlan discloses using ACE inhibitors in co-therapy in patients susceptible to congestive heart failure. Applicants respectfully traverse this rejection.

Claims 4 and 10 recite a method and composition for preventing congestive heart failure in a patient not previously having congestive heart failure and who has an essentially maintained heart function. Those skilled in the art understand that the determination of whether a patient does or does not have an "essentially maintained heart function" depends on the left ventricular ejection fraction of the patient's heart. The patients treated in Maclaughlan are disclosed as having symptomatic heart failure and an ejection fraction of $\leq 35\%$. See page 18, lines 24-25. Those skilled in

the art understand that an ejection fraction of $\leq 35\%$ reflects left ventricular systolic dysfunction and a heart function that is not "essentially maintained." Thus, the disclosed treatments in Maclaughlan do not anticipate the present invention. Furthermore, nothing in Maclaughlan would have motivated one skilled in the art to disregard the chosen patient selection criteria and instead administer the compounds to patients having more favorable ejection fraction measurements and perhaps having essentially maintained heart functions. The present invention is thus unobvious over Maclaughlan as well.

The Examiner also rejected composition claims 14 and 15 under 35 U.S.C. § 102(b) as anticipated by an FDA Orange Book Active Ingredient Detail Record Search. The Orange Book compositions cited by the Examiner do not teach compositions for the prevention of congestive heart failure as recited in the claims. Instead, applicants believe that the cited compositions from the Orange Book are indicated for the treatment of hypertension. Applicants therefore respectfully request that the Examiner withdraw this rejection.

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V. Rejection under 35 U.S.C. § 103

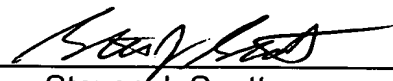
The Examiner rejected claims 8 and 9 at least as they were directed to the prevention of diabetes in light of Tschollar. Applicants do not acquiesce in the conclusion of unpatentability reached by the Examiner. Nonetheless, and as explained above, applicants have canceled claims directed to the prevention of diabetes, rendering this rejection moot. Applicants retain the right to pursue the canceled subject matter in a separate patent application.

In light of the above, the pending claims should be in condition for allowance.
If there is any fee due in connection with the filing of this Amendment, please charge
the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: December 20, 2001

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Appendix Detailing Amendments to Claims

4. (Amended) A method of preventing congestive heart failure in a patient not previously having congestive heart failure and who has an essentially maintained heart function, comprising administering to said patient an effective amount of an inhibitor of the renin-angiotensin system [or a pharmaceutically acceptable derivative thereof].

5. (Amended) A method of claim [1, 3, or] 4, wherein the inhibitor of the renin-angiotensin system is an angiotensin converting enzyme inhibitor, or an angiotensin II type 1 receptor antagonist [, or a pharmaceutically acceptable derivative of any of these].

6. (Amended) A method of claim 5, wherein the angiotensin converting enzyme inhibitor is alacepril, alatriopril, altiopril calcium, ancovenin, benazepril, benazepril hydrochloride, benazeprilat, benzoylcaptopril, captopril, captopril-cysteine, captopril-glutathione, ceranapril, ceranopril, ceronapril, cilazapril, cilazaprilat, delapril, delapril-diacid, enalapril, enalaprilat, enapril, epicaptopril, foroxymithine, fosfenopril, fosenopril, fosenopril sodium, fosinopril, fosinopril sodium, fosinoprilat, fosinoprilic acid, glycopril, hemorphin-4, idrapril, imidapril, indolapril, indolaprilat, libenzapril, lisinopril, lyciumin A, lyciumin B, mixanpril, moexipril, moexiprilat, moveltipril, muracein A, muracein B, muracein C, pentopril, perindopril, perindoprilat, pivalopril, pivopril, quinapril, quinapril hydrochloride, quinaprilat, ramipril, ramiprilat, spirapril, spirapril hydrochloride, spiraprilat, spiropril, spiropril hydrochloride, temocapril, temocapril hydrochloride, teprotide,trandolapril, trandolaprilat, utibapril, zabicipril, zabiciprilat, zofenopril, or zofenoprilat [, or a pharmaceutically acceptable derivative thereof].

7. (Amended) The method of claim 6, wherein the angiotensin converting enzyme inhibitor is ramipril, ramiprilat, lisinopril, enalapril, or enalaprilat [, or a pharmaceutically acceptable derivative thereof].

8. (Amended) The method of claim 5, wherein the angiotensin II antagonist is candesartan, candesartan cilexetil, losartan, valsartan, irbesartan, tasosartan, telmisartan, or eprosartan [, or a pharmaceutically acceptable derivative thereof].

9. (Amended) The method of claim 8, wherein the angiotensin II antagonist is candesartan, or candesartan cilexetil [, or a pharmaceutically acceptable derivative thereof].

10. (Amended) A pharmaceutical composition for preventing [stroke, diabetes and/or,] congestive heart failure in a patient not previously having congestive heart failure and who has an essentially maintained heart function, comprising a therapeutically effective amount of an inhibitor of the renin-angiotensin system to prevent the congestive heart failure in the patient and [, or a pharmaceutically acceptable derivative thereof, with] a pharmaceutically acceptable carrier.

11. (Amended) A pharmaceutical composition of claim 10, wherein the inhibitor of the renin-angiotensin system is an angiotensin converting enzyme inhibitor, or an angiotensin II type 1 receptor antagonist [, or a pharmaceutically acceptable derivative of any of these].

12. (Amended) A pharmaceutical composition of claim 11, wherein the angiotensin converting enzyme inhibitor [or a pharmaceutically acceptable derivative thereof] is alacepril, alatriopril, altiopril calcium, ancovenin, benazepril, benazepril hydrochloride, benazeprilat, benzoylcaptopril, captopril, captopril-cysteine, captopril-glutathione, ceranapril, ceranopril, ceronapril, cilazapril, cilazaprilat, delapril, delapril-diacid, enalapril, enalaprilat, enapril, epicaptopril, foroxymithine, fosfenopril, fosenopril, fosenopril sodium, fosinopril, fosinopril sodium, fosinoprilat, fosinoprilic acid, glycopril, hemorphin-4, idrapril, imidapril, indolapril, indolaprilat, libenzapril, lisinopril, lyciumin A, lyciumin B, mixanpril, moexipril, moexiprilat, moveltipril, muracein A, muracein B, muracein C, pentopril, perindopril, perindoprilat, pivalopril, pivopril, quinapril, quinapril hydrochloride, quinaprilat, ramipril, ramiprilat, spirapril, spirapril hydrochloride, spiraprilat, spiropril, spiropril hydrochloride, temocapril, temocapril hydrochloride, teprotide, trandolapril, trandolaprilat, utibapril, zabicipril, zabiciprilat, zofenopril or zofenoprilat.

13. (Amended) A pharmaceutical composition of claim 12, wherein the angiotensin converting enzyme inhibitor is ramipril, ramiprilat, lisinopril, enalapril or enalaprilat [or a pharmaceutically acceptable derivative thereof].

14. (Amended) A pharmaceutical composition of claim 11, wherein the angiotensin II antagonist is candesartan, candesartan cilexetil, losartan, valsartan, irbesartan, tasosartan, telmisartan, or eprosartan [or a pharmaceutically acceptable derivative thereof].

15. (Amended) A pharmaceutical composition of claim 14, wherein the angiotensin II antagonist is candesartan, or candesartan cilexetil [, or a pharmaceutically acceptable derivative thereof].